

09/786502

FILE 'REGISTRY' ENTERED AT 10:25:44 ON 10 JAN 2005  
L1 5 SEA ABB=ON PLU=ON GCGGCCGCAATTGAAGTTATGTATCCT|TCGAGGATCTTGTCA  
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FILE 'CAPLUS' ENTERED AT 10:27:05 ON 10 JAN 2005  
L2 2 SEA ABB=ON PLU=ON L1

L2 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2002:123513 CAPLUS  
DOCUMENT NUMBER: 136:182467  
TITLE: Fusion proteins comprising anti-GD2 scFv and signal  
domain and transmembrane domain of human CD28 for  
treating cancer  
INVENTOR(S): Sadelain, Michel; Cheung, Nai-Kong V.; Krause, Anja;  
Guo, Hong-Fen  
PATENT ASSIGNEE(S): USA  
SOURCE: U.S. Pat. Appl. Publ., 9 pp., Cont.-in-part of Appl.  
No. PCT/US97/04427.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002018783	A1	20020214	US 1997-940544	19970930
WO 9734634	A1	19970925	WO 1997-US4427	19970320
W: CA, JP, MX, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRIORITY APPLN. INFO.:			WO 1997-US4427	A2 19970320
			US 1996-13703P	P 19960320

AB Genetically-modified T cells with enhanced survival in vivo are obtained by transducing T cells with a recombinant polynucleotide encoding a fusion protein comprising a single chain Fv antibody (comprising the variable regions of the heavy and light chains of a selected antibody such as an anti-GD2 antibody) linked to CD28 receptor. T cells expressing this recombinant fusion protein exhibit enhanced survival when reintroduced to an in vivo environment.. These T cells can be used to induce an immune response to cells, particularly tumor cells, when express the antigen for which the antibody is specific. Cells expressing recombinant fusion proteins according to the invention can also be used for in vitro purging of stem cells/bone marrow and for in vivo targeting of tumor cells and other antigen-bearing cells for purposes of imaging.

IT Hybridoma  
(5F11 and 3G6; T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)  
IT Cell activation  
(T cell; T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)  
IT Antitumor agents  
Brain, neoplasm  
DNA sequences  
Imaging

Melanoma

Molecular cloning

Sarcoma

T cell (lymphocyte)

(T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)

IT Antibodies and Immunoglobulins

Fusion proteins (chimeric proteins)

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)

IT TCR (T cell receptors)

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)

IT CD28 (antigen)

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)

IT T cell (lymphocyte)

(activation; T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)

IT Animal cell

(antigen-bearing; T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)

IT T cell (lymphocyte)

(cytotoxic; T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)

IT Antibodies and Immunoglobulins

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(fragments, scFv; T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)

IT Antibodies and Immunoglobulins

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(heavy chain; T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)

IT Signal peptides

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(human CD28; T cells expressing polynucleotide encoding fusion proteins)

- comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)
- IT Antibodies and Immunoglobulins  
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (light chain; T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)
- IT Antibodies and Immunoglobulins  
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (monoclonal; T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)
- IT Nerve, neoplasm  
 (neuroblastoma; T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)
- IT Bone marrow  
 Stem cell  
 (purging; T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)
- IT Lung, neoplasm  
 (small-cell carcinoma; T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)
- IT Gene  
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (suicide; T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)
- IT Antigens  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (surface; T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)
- IT Neoplasm  
 (targeting; T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)
- IT Bone marrow  
 (toxicity, purging; T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)
- IT Protein motifs  
 (transmembrane domain, human CD28; T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)
- IT Antigens  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (tumor-associated, surface; T cells expressing polynucleotide encoding

fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)

IT 65988-71-8, Ganglioside GD2  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (T cell expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)

IT 399598-54-0P 399598-55-1P  
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (nucleotide sequence; T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)

IT 9002-06-6, Thymidine kinase  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (suicide gene encoding; T cells expressing polynucleotide encoding fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)

IT 399598-81-3 **399598-82-4**  
 RL: PRP (Properties)  
 (unclaimed sequence; fusion proteins comprising anti-GD2 scFv and signal domain and transmembrane domain of human CD28 for treating cancer)

L2 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:175953 CAPLUS

DOCUMENT NUMBER: 132:217131

TITLE: Fusion proteins with single-chain antibody to prostate-specific membrane antigen and methods for treatment of prostate cancer

INVENTOR(S): Sadelain, Michel; Bander, Neil H.; Gong, Michael

PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA

SOURCE: PCT Int. Appl., 25 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000014257	A1	20000316	WO 1999-US20349	19990903
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2343156	AA	20000316	CA 1999-2343156	19990903
EP 1109921	A1	20010627	EP 1999-945508	19990903
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002524081	T2	20020806	JP 2000-568998	19990903
PRIORITY APPLN. INFO.:			US 1998-99138P	P 19980904
			WO 1999-US20349	W 19990903

AB A fusion receptor composition which is effective to promote a cellular immune

response to prostate-specific membrane antigen (PSMA) in vivo when the fusion receptors is expressed by T lymphocytes has the structure: PSMA-scFv: connector: cytoplasmic domain. The PSMA-scFv in this structure is a single chain antibody cloned from the V region genes of a hybridoma specific for PSMA. The connector region is provided to give a spacing between the OSMA-scFv and the cytoplasmic domain, such that both can retain substantial function. A suitable connector is the CD8 hinge, although other connectors of greater or lesser length might be used. The cytoplasmic domain is included to direct the function of the fusion receptor. One exemplary cytoplasmic domain which can be used in the fusion receptor of the invention is a T cell receptor  $\zeta$ -chain cytoplasmic domain. An expression vector encoding the fusion receptor is transduced into primary T lymphocytes obtained from an individual to be treated. The transduced lymphocytes are returned to the patient where cells expressing the fusion receptor secrete interleukin 2 and proliferate in response to PSMA-pos. cells. The resulting cytotoxic lymphocytes specifically lyse cells expressing PSMA and thus can be used to target PSMA-pos. tumor cells and neovasculature.

IT Receptors

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(4-1BB, cytoplasmic domain of, fusion proteins with anti-PSMA scFv; fusion proteins with single-chain antibody to prostate-specific membrane antigen and methods for treatment of prostate cancer)

IT Retroviral vectors

(SFG, scFv fusion protein expression vector; fusion proteins with single-chain antibody to prostate-specific membrane antigen and methods for treatment of prostate cancer)

IT CD28 (antigen)

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(cytoplasmic domain of, fusion proteins with anti-PSMA scFv; fusion proteins with single-chain antibody to prostate-specific membrane antigen and methods for treatment of prostate cancer)

IT Prostate-specific antigen

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(fusion proteins with single-chain antibody to prostate-specific membrane antigen and methods for treatment of prostate cancer)

IT CD8 (antigen)

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(linker peptide from, fusion proteins with anti-PSMA scFv; fusion proteins with single-chain antibody to prostate-specific membrane antigen and methods for treatment of prostate cancer)

IT Prostate gland

Prostate gland  
(neoplasm, inhibitors; fusion proteins with single-chain antibody to prostate-specific membrane antigen and methods for treatment of prostate cancer)

IT Lymphocyte

(peripheral blood; fusion proteins with single-chain antibody to prostate-specific membrane antigen and methods for treatment of prostate cancer)

IT Antitumor agents

(prostate gland; fusion proteins with single-chain antibody to prostate-specific membrane antigen and methods for treatment of prostate cancer)

IT Genetic vectors

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(scFv fusion protein expression vector; fusion proteins with single-chain antibody to prostate-specific membrane antigen and methods for treatment of prostate cancer)

IT Antibodies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(scFv, anti-PSMA, fusion proteins; fusion proteins with single-chain antibody to prostate-specific membrane antigen and methods for treatment of prostate cancer)

IT CD3 (antigen)  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
( $\zeta$ -chain of, fusion proteins with anti-PSMA scFv; fusion proteins with single-chain antibody to prostate-specific membrane antigen and methods for treatment of prostate cancer)

IT 131995-90-9 131996-12-8 155424-19-4 261345-87-3, 4: PN: WO0014257 SEQID: 4 unclaimed DNA 261345-88-4, 5: PN: WO0014257 SEQID: 5 unclaimed DNA 261345-89-5, 6: PN: WO0014257 SEQID: 6 unclaimed DNA 261345-90-8, 7: PN: WO0014257 SEQID: 7 unclaimed DNA 261345-91-9, 8: PN: WO0014257 SEQID: 8 unclaimed DNA  
RL: PRP (Properties)  
(unclaimed nucleotide sequence; fusion proteins with single-chain antibody to prostate-specific membrane antigen and methods for treatment of prostate cancer)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

E1 THROUGH E3 ASSIGNED

FILE 'REGISTRY' ENTERED AT 10:28:02 ON 10 JAN 2005  
L3 3 SEA FILE=REGISTRY ABB=ON PLU=ON (261345-90-8/BI OR 261345-91-9/BI OR 399598-82-4/BI)

L4 3 L1 AND L3

L4 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN  
RN 399598-82-4 REGISTRY  
CN DNA, d(T-C-G-A-G-G-A-T-C-T-T-G-T-C-A-G-G-A-G-C-G-A-T-A-G-G-C-T-G-C) (9CI)  
(CA INDEX NAME)

OTHER NAMES:

CN 4: PN: US20020018783 PAGE: 4 unclaimed sequence  
CI MAN  
SQL 30

SEQ 1 tcgaggatct tgtcaggagc gataggctgc  
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HITS AT: 1-30

\*\*RELATED SEQUENCES AVAILABLE WITH SEQLINK\*\*

REFERENCE 1: 136:182467

L4 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN  
RN 261345-91-9 REGISTRY  
CN 8: PN: WO0014257 SEQID: 8 unclaimed DNA (9CI) (CA INDEX NAME)  
CI MAN  
SQL 30

Searcher : Shears 571-272-2528

09/786502

SEQ 1 tcgaggatct tgtcaggagc gataggctgc  
=====

HITS AT: 1-30

\*\*RELATED SEQUENCES AVAILABLE WITH SEQLINK\*\*

REFERENCE 1: 132:217131

L4 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN  
RN 261345-90-8 REGISTRY  
CN 7: PN: WO0014257 SEQID: 7 unclaimed DNA (9CI) (CA INDEX NAME)  
CI MAN  
SQL 27

SEQ 1 gcggccgcaa ttgaagttat gtatcct  
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HITS AT: 1-27

\*\*RELATED SEQUENCES AVAILABLE WITH SEQLINK\*\*

REFERENCE 1: 132:217131

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2005)

L5 0 S L3

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